Clinical disease patterns in a regional Swiss cohort of 34 pyoderma gangrenosum patients

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Clinical Disease Patterns in a Regional Swiss Cohort of 34 Pyoderma Gangrenosum Patients

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Keywords
Pyoderma gangrenosum · Neutrophilia · C-reactive protein · Leukocytosis · Systemic inflammation

Abstract
Background/Aim: Pyoderma gangrenosum (PG) is a rare, neutrophilic dermatosis often associated with an underlying disease, and clinical data or larger studies are rare. ***Methods:*** In this retrospective study, disease characteristics, clinical manifestations, and treatment response were evaluated in a Swiss cohort of PG patients. ***Results:*** In participating centers, 34 cases (21 females) of PG were analyzed based on clinical and histological presentation between 2002 and 2012. The mean age at diagnosis was 61.2 years; 50% of the patients experienced only 1 episode of PG. In 13 cases (out of 20), recurrences occurred during PG therapy; 64.1% showed only 1 lesion simultaneously. The predominant localization was the lower limb (67%). The lesions were disseminated in 26.6%. At the time of diagnosis or recurrence, the mean diameter was 37.6 mm and the mean ulcer size was 10.3 cm^2. C-reactive protein (CRP) was elevated in 73.2%; leukocytosis was present in 58.9% and neutrophilia in 50.9%. At least 1 associated comorbidity was present in 85% (the most prominent being cardiovascular disease). The most often used systemic treatments were steroids (68.3%), cyclosporine A (31.7%), dapsone (31.7%), and infliximab (13.3%), and the most often used topicals were tacrolimus 0.1% (48.3%) and corticosteroids (35%). PG healed completely at discharge in 50.8%. The average time to diagnosis was 8 months, and the mean duration to healing was 7.1 months. ***Conclusion:*** PG is a difficult-to-diagnose skin disease. Here, markers for inflammation such as CRP, leukocytosis, and neutrophilia were elevated in 50–73% of the PG patients.

A.G.A. Kolios and A. Gübeli contributed equally as first authors. L.E. French and A. Cozzio contributed equally as last authors.

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Introduction

Pyoderma gangrenosum (PG) is a rare, idiopathic, neutrophilic dermatosis presenting with sterile and painful skin ulcerations and very rarely extracutaneous involvement of lung, bone, liver, spleen, myocardium, central nervous system, and cornea [1, 2]. The exact pathomechanism remains largely unknown. PG onset has been described in association with different therapies, comorbidities, trauma, or surgery (pathergy phenomenon), which is present in up to 25% of cases [3–6]. Genetic analysis showing mutations of autoinflammatory genes like MEFV, NLRP3, NLRP12, NOD2, LPIN2, and PSTPIP1 as well as overexpression of inflammatory cytokines like IL-1β, IL-17, IL-8, CXCL 1/2/3/16, and RANTES suggests that PG is an autoinflammatory disease [7, 8].

PG can be classified into (I) a mild pustular form, (II) a rapidly progressive, purulent, ulcerative PG, (III) a superficial, vegetative form, and (IV) a bullous form in which bullae occur before the development of ulceration [5, 9]. Additionally, 6 rare variants have been reported: posttraumatic and postoperative, peristomal, genital, extracutaneous neutrophilic disease, pyostomatitis vegetans, and PG of infancy and childhood [10–12].

An underlying systemic disease is reported in up to 75% of cases, including inflammatory bowel disease (IBD), endocrine disorders including diabetes, hematological, autoimmune-mediated, or rheumatological disorders, and nonhematological malignant diseases [4, 13, 14]. For IBD it could be shown that PG is not necessarily related to the activity of the underlying disease [15].

PG is often misdiagnosed at first manifestation and remains a diagnosis of exclusion. The broad differential diagnosis of ulcerative lesions, especially infectious diseases, must be ruled out. Histology is not specific but shows a sterile neutrophilic infiltrate, mixed inflammation, or lymphocytic vasculitis, which may give a hint towards PG. Su et al. [16] and von den Driesch [17] suggested criteria for PG diagnosis. Two major and at least 2 minor criteria have to be fulfilled. The criteria of Su et al. [16] are as follows: major criteria: (1) rapid progression of a painful, necrotic cutaneous ulcer with irregular violaceous undermined border, and (2) exclusion of relevant differential diagnosis; minor criteria include (a) pathergy in the patient's history or cribriform scarring upon clinical examination, (b) presence of associated disease, (c) histology with sterile dermal neutrophilia, mixed inflammation, or lymphocytic vasculitis, and (d) response to systemic steroid therapy. The criteria of von den Driesch are the following: major criteria: (1) occurrence of a primary sterile, chronic ulceration, typically with violaceous undermined borders, and (2) exclusion of relevant differential diagnosis; minor criteria include (a) histology from borders of the ulceration revealing dermal neutrophilia with vasculitis and immunoglobulin deposits or complement factor deposits in the vessels, (b) presence of associated disease, and (c) response to systemic immunosuppressive therapy, with little or no response to conventional external ulcer therapies.

The most frequently reported topical treatments include tacrolimus and topical and intralesional corticosteroids. Nicotine cream and pimecrolimus are also often used and occasionally sodium cromoglycate [18, 19]. Other topicals have also been reported to be effective but the level of evidence is low: intralesional cyclosporine A, potassium iodide, nitrogen mustard, platelet-derived growth factor, recombinant human epidermal growth factor, hyperbaric oxygen, and surgical repair by graft or flap. In a case series of 6 patients it was found that the topical coagulation factor XIII also exerts beneficial effects on the tissue regeneration and wound healing in recalcitrant PG [20]. Systemically different schemes have been suggested – widely accepted are corticosteroids +/– cyclosporine A as 1st-line therapy [21] and dapsone as 2nd-line therapy. Other treatments including TNF-α inhibitors (infliximab, adalimumab, etanercept), thalidomide, tacrolimus, cyclophosphamide, azathioprine, mycophenolate mofetil, clofazimine, IVIG, GM-CSF, colchicine, and methotrexate have been reported as 3rd-line therapies [2, 5, 6, 14, 15, 22–24]. Recently, we showed that canakinumab (monoclonal anti-IL-1b antibody) is effective in steroid-refractory PG as well as we and others for ustekinumab (anti-IL-12/IL-23 monoclonal antibody) [25–27]. In addition of the above therapies, control of the underlying associated disease could have a positive effect on the PG course [15].

In this retrospective study, we evaluated the disease characteristics, clinical manifestations, laboratory values, and treatment outcomes of a cohort of PG patients from 2 major hospitals in Switzerland between January 2002 and December 2012.

Material and Methods

For further details, see the supplementary material (see www.karger.com/10.1159/000481432 for all online suppl. material) [16, 17] (Fig. 1).

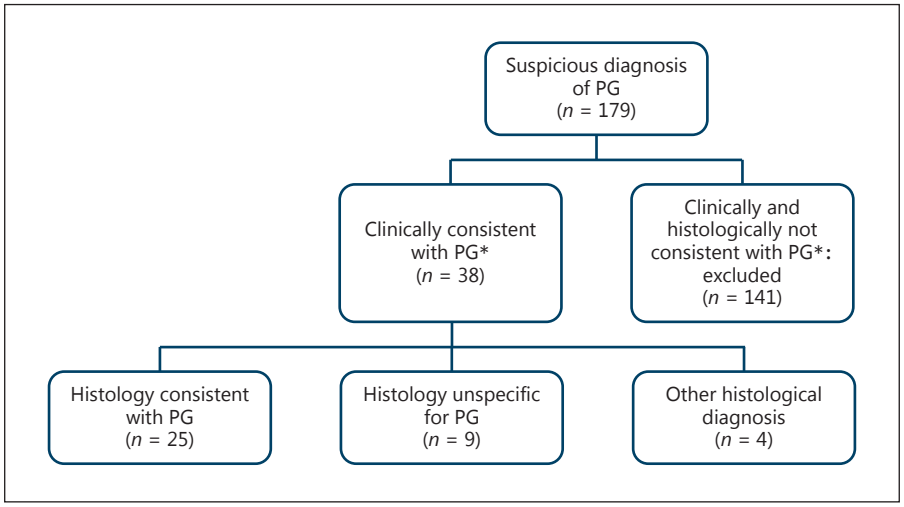

Fig. 1. Flowchart of Materials and Methods. Decision tree of pyoderma gangrenosum (PG) inclusion. * According to the criteria of Su et al. [16].

Table 1. Demographics: patient characteristics

Total number of patients, *n* (%)	34 (100)
Male, *n* (%)	13 (38.2)
Female, *n* (%)	21 (61.8)
Gender ratio (F:M)	1.6:1
Mean age (±SD), years	65.9±18.5
Mean age at manifestation (±SD), years	61.2±17.8
Mean height, m	1.7
Mean weight, kg	67
Mean BMI	24.1
Smoking (yes), *n* (%)	7 (20.6)
Alcohol (yes), *n* (%)	4 (11.8)

Demographic analysis of the pyoderma gangrenosum cohort.

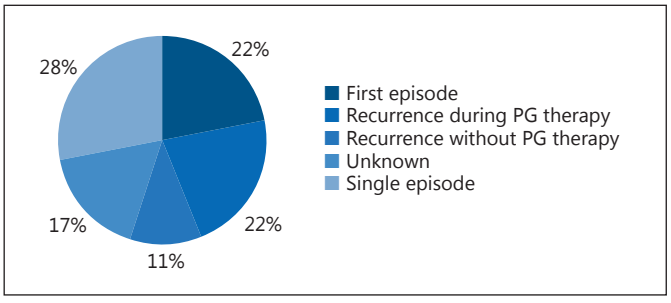

Fig. 2. Recurrence of disease. Disease course divided into patients with only a single pyoderma gangrenosum (PG) episode, recurrent disease with first episodes, and variable recurrences by onset during or without PG therapy.

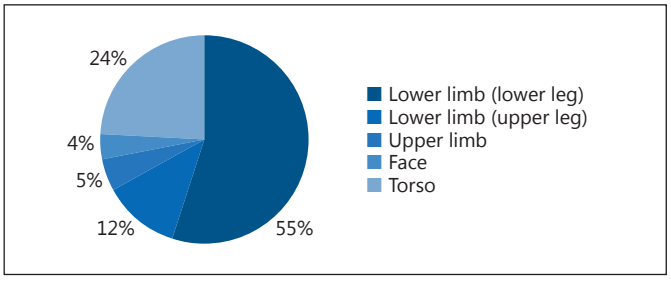

Fig. 3. Pyoderma gangrenosum lesion localization by body area.

Results

Between 2002 and 2012, a total of 34 cases of diagnosed PG (14 from University Hospital Zurich, 5 from the private practice of Prof. Werner Kempf, and 15 from Kantonsspital St. Gallen) were included in the study. Of the 34 patients, 21 were female (61.8%, female:male ratio 1.6:1), and the mean age at time of diagnosis was 61.2 years (range, 18–86 years). The mean BMI was 24.1 (range, 17.4–32.1). Nicotine and alcohol consumption was documented in 20.6 and 11.8% of patients, respectively (Table 1).

In total, 60 admissions of PG with a mean number of 1.9 lesions per patient (range, 1–7) were documented, with a female predominance of 2.2 versus 1.5 admissions. Of the 60 admissions, 17 (50% of patients) were due to only 1 flare. In 10 admissions follow-up information was not available. The remaining patients showed a first episode (13 admissions) with repetitive recurrent disease either during (13 admissions) or without therapy (7 admissions). Pathergy phenomenon was reported in 16 patients (47%) (Fig. 2). Only 1 lesion was present in 61.7% (37 admissions), 2–4 lesions in 28.3% (17 admissions), 5–7 lesions in 8.3% (5 admissions), and more than 7 lesions

Table 2. Laboratory values (CRP, leukocytes, neutrophils) of the pyoderma gangrenosum cohort

CRP (Ref. <5 mg/L)	
<5 mg/L	15 (26.8)
5–40 mg/L	22 (39.3)
41–200 mg/L	11 (19.6)
>200 mg/L	8 (14.3)
Available CRP values on admission, *n* (%)	56 (100)
Median CRP (±SD), mg/L	14.5±92.5
Leukocytes (Ref. 3.0–9.6 × 10^9/L)	
<3.5 × 10^9/L	0 (0.0)
3.5–9.6 × 10^9/L	23 (41.1)
9.7–20 × 10^9/L	27 (48.2)
>20 × 10^9/L	6 (10.7)
Available leukocyte counts on admission, *n* (%)	56 (100)
Median leukocytes (±SD), × 10^9/L	10.5±13.2
Neutrophils (Ref. 1.4–8.0 × 10^9/L)	
<1.4 × 10^9/L	0 (0.0)
1.4–8.0 × 10^9/L	28 (49.1)
8.1–20 × 10^9/L	22 (38.6)
>20 × 10^9/L	7 (12.3)
Available neutrophil counts on admission, *n* (%)	57 (100)
Median neutrophils (±SD), × 10^9/L	8.36±15.1

Data are presented as number of admissions (%) unless otherwise indicated.

in 1.7% (1 admission). The average time to diagnosis was 8.1 months (±18.5 months, range, 0–88 months).

At the time of diagnosis or recurrence, information was available in 56 admissions about lesion size, with a mean diameter of 37.6 mm and a mean ulcer size of 10.3 cm^2 (total 67 lesions): 2 lesions (3%) measured under 10 mm, 36 (53.7%) 10–30 mm, 22 (32.8%) 31–60 mm, and 7 (10.4%) over 60 mm.

In total, 115 PG lesions were recorded, the most common site being the lower limb (67.0%: 54.8% on the lower leg and 12.2% on the thigh) followed by the upper body (24.3%), the upper limbs (5.2%), and the face (3.5%) (Fig. 3). In 26.6% of cases PG occurred simultaneously in at least 2 separate anatomical sites. Postoperatively, 8 lesions appeared, of which 5 occurred after cesarean section. Eight PG lesions (7%, 4 females with 7 episodes and 1 male) developed posttraumatically following acupuncture, punch biopsy, insect bite, or direct accidental blunt trauma.

C-reactive protein (CRP) values were available in 41 admissions, with 73.2% having elevated CRP values: 15 had a value of 5 mg/L or lower (26.8%, normal), 22 between 5 and 40 mg/L (39.3%), 11 between 41 and 200 mg/L (19.6%), and 8 over 200 mg/L (14.3%) (reference value <5 mg/L). Leukocyte counts were available in 41 admissions, with 58.9% having leukocytosis: 41.1% between 3.5 and 9.6 × 10^9/L (normal), 48.2% between 9.7 and 20 × 10^9/L, and 6 over 20 × 10^9/L, with a mean leukocyte concentration of 10.5 × 10^9/L (reference value 3.5–9.6 × 10^9/L). Neutrophil counts were available in 41 admissions, with 50.9% showing neutrophilia (reference value 1.4–8.0 × 10^9/L): 49.1% between 1.4 and 8.0 × 10^9/L (normal), 38.6% between 8.1 and 20 × 10^9/L, and 12.3% over 20 × 10^9/L. Neutropenia or leukopenia were not found in any patient (Table 2).

Comorbidity was found in 29 of 34 patients (85%) (Table 3). Cardiovascular diseases showed the highest prevalence and were observed in 79.4% of patients. Hematological diseases were present in 23.5%, autoimmune or inflammatory diseases in 17.6%, IBD in 14.7%, rheumatological diseases in 35.3%, nonhematological malignancies in 14.7% (2 breast, 1 ovarian, 1 prostate cancer, and 1 precancerous cervical lesion), pulmonary disease in 8.8%, allergies in 20.6%, renal insufficiency in 20.6%, psychiatric diseases in 8.8%, and chronic infections (like status posthepatitis B or C/others) in 8.8% of patients. More than one comorbidity was seen in 15 patients (44.1%). No associated comorbidity was seen in 5 patients (15%). None of our patients showed extracutaneous PG involvement.

Tacrolimus 0.1% ointment was used in 48.3% of all admissions, topical antimicrobial agents were used in

Table 3. Comorbidities (n = 34 patients)

		Total		Age 15–54		Age 55–74		Age 75+	
		counts	%	counts	%	counts	%	counts	%
Inflammatory bowel disease		5	14.7	2	5.9	0	0.0	3	8.8
	Crohn disease	3	8.8	2	5.9	0	0.0	1	2.9
	Colitis indeterminata	1	2.9	0	0.0	0	0.0	1	2.9
	Colitis ulcerosa	1	2.9	0	0.0	0	0.0	1	2.9
Cardiovascular diseases		27	79.4	2	5.9	5	14.7	19	55.9
	Arterial hypertension	10	29.4	0	0.0	1	2.9	9	26.5
	Peripheral obstructive arterial disease	2	5.9	0	0.0	1	2.9	1	2.9
	Hypertensive heart disease	4	11.8	0	0.0	0	0.0	4	11.8
	Myocardial infarction	2	5.9	0	0.0	0	0.0	2	5.9
	Cardiopathy of unknown origin	1	2.9	0	0.0	1	2.9	0	0.0
	Cerebrovascular infarction	1	2.9	0	0.0	1	2.9	0	0.0
	Diabetes mellitus	3	8.8	0	0.0	0	0.0	3	8.8
	Thrombosis	3	8.8	2	5.9	0	0.0	0	0.0
	Metabolic syndrome	1	2.9	0	0.0	1	2.9	0	0.0
Rheumatological conditions		12	35.3	1	2.9	2	5.9	7	20.6
	Rheumatoid arthritis	1	2.9	0	0.0	0	0.0	1	2.9
	Polymyalgia rheumatica	1	2.9	0	0.0	0	0.0	1	2.9
	Sclerodermia	1	2.9	0	0.0	1	2.9	0	0.0
	Arthralgia/others	5	14.7	0	0.0	1	2.9	3	8.8
	Osteopenia/porosis	4	11.8	1	2.9	0	0.0	2	5.9
Hematological disorder		8	23.5	1	2.9	3	8.8	4	11.8
	MGUS	3	8.8	1	2.9	1	2.9	1	2.9
	Waldenström disease	1	2.9	0	0.0	0	0.0	1	2.9
	Megaloblastic macrocytic anemia	2	5.9	0	0.0	1	2.9	1	2.9
	Spherocytosis	1	2.9	0	0.0	1	2.9	0	0.0
	Lymphoplasmacytic B-cell lymphoma	1	2.9	0	0.0	0	0.0	1	2.9
Inflammatory/autoimmune mediated conditions		6	17.6	1	2.9	3	8.8	2	5.9
	Psoriasis vulgaris	2	5.9	1	2.9	0	0.0	1	2.9
	Antiphospholipid syndrome	2	5.9	0	0.0	1	2.9	1	2.9
	Leukocytoclastic vasculitis	1	2.9	0	0.0	1	2.9	0	0.0
	Hypothyreosis Hashimoto	1	2.9	0	0.0	1	2.9	0	0.0
Malignancy – nonhematological		5	14.7	1	2.9	2	5.9	2	5.9
COPD		3	8.8	0	0.0	0	0.0	3	8.8
Allergies		7	20.6	3	8.8	1	2.9	2	5.9
Renal insufficiency		7	20.6	0	0.0	2	5.9	5	14.7
Psychiatric diagnosis		3	8.8	1	2.9	0	0.0	1	2.9
Hepatitis B/C, other		3	8.8	1	2.9	2	5.9	0	0.0
Multiple comorbidities		15	44.1	2	5.9	4	11.8	9	26.5

Comorbidities by age (15–54, 55–74, 75+ years) and group (inflammatory bowel disease, cardiovascular, rheumatological, hematological, inflammatory/autoimmune, and others).

Table 4. Topical and systemic treatments

		Admissions	
		n	%
Topical/intralesional steroids	Total	21	35.0
Topical antimicrobials	Octenidindihydrochloride	7	11.7
	Fusidic acid	6	10.0
	Chloramine T	6	10.0
	Others	11	18.3
	Total	30	50.0
Topical immunosuppressants	Tacrolimus 0.1%	29	48.3
	Infliximab drops	1	1.7
	Total	30	50.0
Other topicals	Hyaluronic acid (2 mg/g)/sulfadiazine (20 mg/g)	5	8.3
	Sodium alginate	5	8.3
	Clostridiopeptidase A	4	6.7
	Others	3	5.0
Systemic steroids (oral/i.v.)	Total	41	68.3
Systemic immunosuppressants	Cyclosporine A	19	31.7
	Azathioprine	5	8.3
	Infliximab	8	13.3
	Etanercept	2	3.3
	Adalimumab	1	1.7
	Canakinumab	4	6.7
	Tacrolimus	3	5.0
	Cyclophosphamide	3	5.0
	Methotrexate	2	3.3
	Mycophenolate mofetil	1	1.7
	Total	48	80.0
Systemic antimicrobials	Dapsone	19	31.7
	Clindamycin	5	8.3
	Others	6	10.0
	Total	30	50.0
Other systemics	IVIG	2	3.3
	Mesalazine	5	8.3

IVIG, intravenous immunoglobulins.

50%, and topical or intralesional steroids were applied in 35%. Overall, 68.3% of patients received systemic steroids, 80% of which were immunomodulatory agents, among them being cyclosporine A (31.7%), dapsone (31.7%), infliximab (13.3%), azathioprine or mesalazine (8.3%), and canakinumab (6.7%) (Table 4). Overlapping treatment indications for PG and, for example, underlying IBD, as well as contraindications for PG treatments like TNF inhibitors, were taken into account. Side effects due to systemic therapy were reported in 14 patients (41.2%; online suppl. Table 1). A surgical procedure was performed in 27.9% of all admissions (17 patients: 4 debridements, 4 debridements + VAC therapy, 2 debridements + Epidex® application, and 7 debridements + split-thickness skin graft transplantations). Systemic corticosteroids or immunomodulatory therapy were concomitantly used in 35.3% of the surgical procedures (no additional therapy in 23.5%, unknown in 41.2%).

In 50.8% of all admissions (61 admissions in total) the PG healed completely until discharge from the hospital, in 47.5% a PG lesion was still present at discharge, and 1 patient (1.7%) died due to *Pseudomonas aeruginosa* sepsis. The mean time to complete ulcer healing was 7.1 months (range, 1–30 months) according to healed PG until discharge. If, when, and how PG healed in nonhospital settings cannot be evaluated due to nonavailable data. In detail, 21 patients (61.8%) received a combination treatment with topicals and systemics at least on one occasion; 46% of the completely resolved PG lesions had been treated with topical steroids, 46% with tacrolimus 0.1% ointment, and 6.6% with intralesional steroids. In cases which resulted in complete resolution, systemic steroids was the therapy used in 68.8%, cyclosporine A in 29.5%, dapsone in 29.5%, infliximab in 16.4%, and surgical intervention in 26.2% of cases.

Discussion

PG is a rare, neutrophil-mediated disease characterized by painful skin ulceration. Extracutaneous manifestations are very rare and were not present in any of our patients. Over a 10-year period, 34 patients with a diagnosis of PG fulfilling the criteria suggested by Su et al. [16] and von den Driesch [17] were reviewed. We found a female predominance of 1.6:1, a mean age of manifestation of 61.2 years, a pathergy phenomenon in 16 patients (47%), and the lower limbs as the most frequently affected anatomic sites, all of which are consistent with other reports [3, 4, 17, 28–34]. The average number of PG flares was 1.9, which is lower than previously reported, but women showed more frequent recurrences than men (2.2 vs. 1.5) [31]. A single PG lesion was the most frequent clinical presentation and seen in 37 admissions (61.7%), with a mean diameter of 37.6 mm and a mean ulcer size of 10.3 cm^2; as previously reported, more than half of the lesions had a size ranging between 10 and 30 mm in diameter [31].

The mean CRP level of 14.5 mg/L is lower than previously reported by Saracino et al. [30]. The mean leucocyte and neutrophil counts were 10.5×10^9/L and 8.36×10^9/L, respectively. This is the first study reporting evidence of elevated CRP, neutrophilia, and leukocytosis in PG patients, which is indicative of systemic inflammation in PG patients, as is more and more suggested in the field [35]. However, potential bias with regard to these data is that, retrospectively, a causative or coexistent infection could not be fully ruled out.

Overall, 79.4% of our patients suffered from associated disease, which is in the upper range of previous reports (33–79%) [2, 36]. IBD was present in 14.7% of cases compared to 8.7–34% in previous reports [28, 36], and IgA MGUS was present in 8.8% compared to 15% [13]. Interestingly, we found that 79.4% of patients had a cardiovascular disease, with 55.9% of all patients being over 75 years of age. In the Swiss population, the prevalence of arterial hypertension in patients over 75 years ranges from 50 to 56% and diabetes ranges from 9 to 18% [37]. Both arterial hypertension and diabetes mellitus were less frequent in our patients over 75 years, with 29.4 and 8.8%, respectively. In our cohort, cardiovascular comorbidities including diabetes mellitus did not appear more frequently than in an age-matched control group. Due to the relatively low number of patients in our cohort, it is difficult to conclude whether there is a relationship between PG and this comorbidity or just an unrelated age-typical appearance.

Prior to study inclusion, we also performed a re-evaluation of all 38 biopsies, which led to the exclusion of 3 patients showing features of Martorell hypertensive ischemic leg ulcer (HYTILU) and 1 with morphea. Typical characteristics of HYTILU are an ulceration at the laterodorsal lower leg with central black necrosis and purple inflamed ulcer borders, typically in patients with arterial hypertension (100%) and frequently diabetes mellitus (up to 60%) and metabolic syndrome [38]. If the biopsy taken is too small, the chance of visualizing "PG"-like features and missing the typical features of HYTILU (subcutaneous stenotic arteriolosclerosis in 100% and medial calcification in 71% of cases) is high. A deeper evaluation of HYTILU and PG is currently in preparation.

In our study, PG was most frequently treated with topical tacrolimus (48.3%) as well as topical (35%) or systemic (68.3%) corticosteroids (prednisone starting between 60 and 120 mg daily), either as monotherapy or in combination with steroid-sparing agents such as cyclosporine A, as reported in previous studies [2, 15, 24, 28, 31, 39, 40]. The use of systemic steroids (68.3% of cases) was less frequent than previously reported (80%) [3]. The most frequently used biological was infliximab (13.3%). In 27.9% of our cases a surgical intervention was performed, but a concomitant immunosuppressive therapy was used in only 35.3%. Surgical treatment has been discussed controversially due to the risk of a pathergy phenomenon. However, more recent studies do not suggest elevated pathergy following surgery when combined with immunosuppression; on the contrary, up to 60% of patients show either complete or partial healing [29, 30].

In 51% of the PG episodes complete ulcer healing corresponding to complete remission occurred within a mean time of 7.1 months. In previous studies complete disease remission was reported in 69–72% of cases within 3.9–15.5 months and in 95% within 3 years [3, 9, 30, 31]. In our study, due to the lack of follow-up data, the rate and time to complete remission in patients with incompletely healed ulcers at discharge is not known. Overall, only 1 patient with PG died due to *P. aeruginosa* sepsis, which resulted in a mortality rate of 2.6%. The published average mortality rate in PG varies from 6 to 30% [23, 29, 31]. A possible bias might be a shorter follow-up time in our cohort compared to published studies. The time to diagnosis is often prolonged in PG, and we found 8.1 months to be the average time from first manifestation to diagnosis. We did not find comparable data from other studies.

PG is a rare disease with an estimated incidence of 3–10 patients per million population per year [29]. Therefore, it is important to improve the diagnostic process in cases of unusual skin ulcerations. Early involvement of wound specialists and dermatologists is mandatory to evaluate PG. Exclusion of other ulcerating skin diseases is necessary before making the diagnosis of PG. Optimized management with rapid escalation of therapeutic options in cases of nonresponse or exacerbation should be considered [18]. By showing increased CRP, leukocytosis, and neutrophilia in a considerable proportion of our patients, an expected but not formally proven aspect of PG was identified in this retrospective study. These values have not been analyzed together in previous studies. Further studies, preferably in larger prospective international registries, would help to better characterize this rare disease. A prospective approach may allow blood and skin sampling as well as performing cytokine profiling with the potential to guide the application of targeted therapies.

Key Message

Markers for inflammation like CRP, leukocytosis, and neutrophilia were elevated in this pyoderma gangrenosum cohort. The average time to diagnosis was 8 months, and the mean duration to healing was 7.1 months.

Statement of Ethics

Institutional ethical review board approval was obtained from the local ethics committee (KEK-ZH 2014-0432) before the retrospective study was performed.

Disclosure Statement

None of the authors has any conflict of interest or financial interests related to the article.

Author Contributions

All authors had full access to all of the data in the case. Drs. A.G.A. Kolios, A. Gübeli, and A. Cozzio take responsibility for the integrity of the data and the accuracy of the data analysis. A.G.A. Kolios, A. Cozzio, L.E. French, and B. Meier drafted the manuscript. J.-T. Maul, B. Meier, M. Anliker, E. Guenova, K. Kerl, W. Kempf, T. Kündig, J. Nilsson, J. Hafner, A.A. Navarini, and L.E. French critically revised the manuscript for important intellectual content. L.E. French supervised the study.

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